In the Abstract:

Please substitute the below abstract for the abstract that was filed on November 18, 1999. A marked version of the abstract to show changes made herein is attached as Appendix A.

ABSTRACT

A conjugate, and methods of use of the conjugate, the conjugate having a target seeking group that binds to given cell surface structure and a peptide that (i) contains an amino acid sequence derived from a superantigen, (ii) has the ability of binding to a Vβ chain of a T-cell receptor, and (iii) has a modified ability to bind to a MHC Class II antigen compared to the superantigen from which the peptide is derived, which parts are covalently linked together.

REMARKS

Status of the Claims

- Claims 36-38, 44-47 and 52 are pending in this application
- Claims 36-38, 44-47 and 52 have been rejected by the Examiner

Outstanding Issues

- The Abstract has been object to as allegedly containing new matter.
- Claims 36-38, 44-47 and 52 have been rejected by the Examiner under 35 U.S.C. 103(a) as being allegedly unpatentable over Dohlsten et al., 1991.

Applicants respectfully traverse the outstanding rejections and objections, and Applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

Objection of Abstract under 35 U.S.C. § 132

Applicants have amended the abstract to identify that the two components are covalently linked. This is disclosed in the specification, for example at page 4, lines 5-6. Thus, no new matter has been added and Applicants request withdrawal of the objection.

35 U.S.C. §103(a)

Claims 36-38, 44-47 and 52 have been rejected by the Examiner under 35 U.S.C. 103(a) as being allegedly unpatentable over Dohlsten et al., 1991. Applicants respectfully traverse this rejection and request reconsideration and withdrawal thereof in light of the following remarks.

The Examiner rejected the claimed subject matter under Dohlsten et al. 1991 (PNAS USA 88, 9287-9291) based upon the argument that Dohlsten allegedly suggests making mutations in the C-terminal region of superantigens in order to reduce Class II MHC antigen binding. Applicants respectfully disagree and assert that the claimed invention is not obvious over any prior art of record because, *inter alia*, Dohlsten does not accurately teach or suggest making mutations in any particular region of any superantigens in order to affect Class II MHC antigen binding, including the C-terminal region, and further still, the claimed and supported invention is not limited to making mutations in the C-terminal region of superantigens in order to affect Class II MHC binding.

Applicants remind the Examiner that "before answering Graham's content inquiry, it must be known whether a patent or publication is in the prior art under 35 U.S.C. 102. *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1568, 1 USPQ2d 1593, 1597 (Fed. Cir.), *cert. denied*, 481 U.S. 1025 (1987). Applicants assert that the Dohlsten reference is not "enabling". Applicants refer the Examiner to *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed Cir. 1985) which states even if the claimed invention is disclosed in a printed publication, the disclosure will not suffice as prior art if it was not enabling. Under 35 U.S.C. 102, prior art must sufficiently describe the claimed invention

to have placed the public in possession of it; such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention. *In re LeGrice*, 301 F.2d 939, 133 USPQ 365, 371 (CCPA 1962).

In the Office Action, the Examiner acknowledges that Dohlsten does not teach that the superantigen portion of the conjugate has been mutated to show a modified ability to bind Class II MHC antigen.

However, the Examiner interprets statements in Dohlsten to teach that the class II binding site in superantigens is in the C-terminal region, and that mutations in the C-terminal region of superantigens could reduce class II MHC binding. However, in fact, Dohlsten does not teach that the class II MHC antigen binding site in superantigens is in the C-terminal region, nor does Dohlsten specifically identify amino acids that are necessary for MHC class II binding (and therefore does not suggest that mutations in the superantigens could reduce Class II MHC binding).

The statements in the Dohlsten paper that allegedly teach that mutations in superantigens to reduce MHC class II binding are: i) "it would be of importance to further perturb MHC class II-dependent CTL activity by reducing the binding of the C215-SEA conjugate for MHC class II molecules" (page 9291, column 1) and ii) and "MHC class II binding has been localized to the C-terminal" (page 9291, column 1). These statements, taken alone or in combination, do not in fact teach that class II MHC binding is in the C-terminal region of superantigens. In fact, the next statement on page 9291, column 1 states that "determination of the amino acids necessary for MHC class II binding may provide a rationale to obtain mAb-SEA conjugates with preserve T-cell-activating properties by totally devoid of binding to MHC class II molecules". Thus, Dohlsten is clearly stating that it is not known what amino acids are required for MHC class II binding. Dohlsten does not provide a guideline to determine which amino acids are necessary for binding. All of these statements clearly indicate that the reference is non-enabling for mutating superantigens to modify their ability to bind to MHC class II.

Further, the second statement, "MHC class II binding has been localized to the C-terminal" (page 9291, column 1), is, in fact, not correct when referring to the location for MHC Class II binding on SEC1 and toxin shock syndrome toxin 1. An immense body of work has shown that the MHC class II binding region of SEB (structural homologue of SEC1) and TSST-1 resides in the N-terminal part of the protein and not in the C-terminal (see, e.g., Kim et al., Science, 1994, 266:1870 (co-crystals of MHC class II antigens and TSST-1); and Jardetzky et al., Nature, 1994, 368:711 (SEB and MHC class II binding)). (Please see the Supplemental Information Disclosure Statement submitted herewith).

The present specification (and claimed invention) recognizes and teaches that different regions of superantigens are responsible for binding the MHC class II antigens and that mutations in these regions can affect MHC class II binding. For example, on page 23, lines 12-15 it is stated that, regarding the data and teaching on SEA, "our data indicates an involvement of the four residues N128, H187, H225 and D227".

Thus, in view of the above comments, Applicants assert that the Examiner has not established a *prima facie* case of obviousness to reject the claims under 35 U.S.C. 103(a). *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, (Fed. Cir. 1991). A *prima facie* case necessitates disclosure of the source for either a suggestion or motivation to modify this reference to produce the present invention, and a reasonable expectation of success of producing the present invention. A *prima facie* case must be established by evidence rather than conjecture. *Ex parte Yamamoto*, 575 USPQ2d 1382, 1383, 1384 (CCPA 2000). If anything, Dohlsten demonstrates the need to identify the regions in superantigens that are necessary for MHC class II binding. Applicants assert that it is mere conjecture on the part of the Examiner that one of skill in the art would be able to identify the region without undue experimentation.

Applicants therefore assert that Dohlsten does not render the presently claimed subject matter obvious. Removal of this rejection is therefore respectfully requested.

CONCLUSION

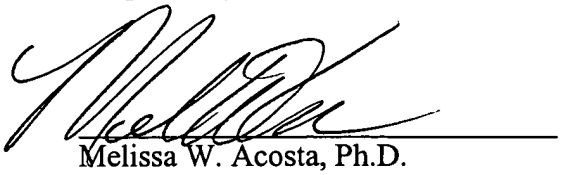
Claims 36-38, 44-47 and 52 are pending in this application. Applicants have attached a marked version of the abstract as Appendix A to show changes made. Applicants assert that no new matter has been added

Applicants have also included a Supplemental Information Disclosure Statement which contains the references cited in the arguments contained herein in response to the Office Action.

Applicants believe that there are no fees associated with the filing of this document. However, the Commissioner is hereby authorized to any required fees associated with this filing, to Deposit Account No. 06-2375, under Order No. 09804877, from which the undersigned is authorized to draw.

Applicants assert that in view of the above remarks, that the application is now considered for allowance. Accordingly, Applicants request that a letter patent be issued on the application as herein amended. If any requirements remain, please contact the undersigned for quick resolution.

Respectfully submitted,



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APPENDIX A: MARKED VERSION OF ABSTRACT

ABSTRACT

A conjugate, and methods of use of the conjugate, the conjugate having a target seeking group that binds to given cell surface structure and a peptide that (i) contains an amino acid sequence derived from a superantigen, (ii) has the ability of [the] binding to a Vβ chain of a T-cell receptor, and (iii) has a modified ability to bind to a MHC Class II antigen compared to the superantigen from which the peptide is derived, which parts are covalently linked together.